

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
28 April 2005 (28.04.2005)

PCT

(10) International Publication Number
WO 2005/037320 A2

(51) International Patent Classification⁷: **A61K 47/48**

(21) International Application Number:
PCT/US2004/026431

(22) International Filing Date: 6 August 2004 (06.08.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/493,389 6 August 2003 (06.08.2003) US

(71) Applicant (*for all designated States except US*): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; National Institutes of Health, Office of Technology Transfer, 6011 Executive Blvd., Suite 325, Rockville, MD 20852-3804 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): JESSOUROUN, Ellen [BR/BR]; Rua Cosme Velho 74, Apt. 1001, Cosme Velho, 22241-090 Rio de Janeiro RJ (BR). DA SILVEIRA, Ivna Alana Freitas, Brasileiro [BR/BR]; Rua

Lopes Quintas, 120 Apt. Bloco 1, Jardim Botanico, 22460-010 Rio de Janeiro, RJ (BR). BASTOS, Renata, Chagas [BR/BR]; Rua Quatis, 234 Taua, Ilha do Governador, 21920-135 Rio de Janeiro, RJ (BR). FRASCH, Carl, E. [US/US]; 13100 Burlwood Drive, Rockville, MD 20853 (US). LEE, Che-Hung, Robert [US/US]; 116 Amberleigh Drive, Silver Springs, MD 20905 (US).

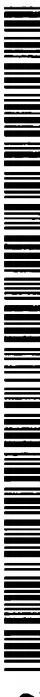
(74) Agent: SIMPSON, Andrew, H.; Knobbe, Martens, Olson and Bear, LLP, 2040 Main Street, Fourteenth Floor, Irvine, CA 92614 (US).

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

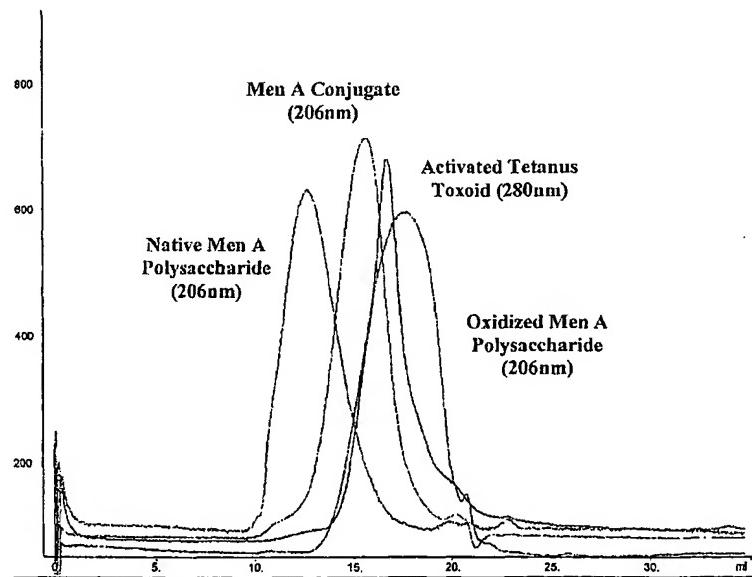
(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH,

[Continued on next page]

(54) Title: PROCESS FOR PREPARING POLYSACCHARIDE-PROTEIN CONJUGATE VACCINES



WO 2005/037320 A2



(57) Abstract: Methods for the manufacture of polysaccharide-protein conjugate vaccines at high yield are provided. The methods involve reaction of a hydrazide group on one reactant with an aldehyde group on the other reactant. The reaction proceeds rapidly with a high conjugation efficiency. Simplified purification processes can be employed to separate the conjugate product from the unconjugated protein and polysaccharide and other small molecule by-products.



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

- *of inventorship (Rule 4.17(iv)) for US only*

Published:

- *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.